INTER-ATRIAL SEPTUM ELECTRODE FOR ATRIAL DEFIBRILLATION

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Related Applications

This application is a divisional of United States Patent Application Serial Number 09/827,535 filed on April 6, 2001 which application claims the benefit of United States provisional application serial number 60/196,722, filed April 13, 2000, the disclosures of which are incorporated by reference herein in their entireties.

Government Support

This invention was made with Government support under National Institute of Health grant HL-42760. The Government has certain rights to this invention.

Field of the Invention

This invention relates to methods, apparatus, and catheters that may be used to administer a therapeutic electrical pulse, such as an atrial defibrillation pulse, to the heart of a patient in need of such treatment.

Background of the Invention

Atrial fibrillation (AF) is the most common arrhythmia in humans and represents a significant public health problem. There are presently 2.2 million cases of AF in the United States and approximately 160,000 new cases diagnosed each year. AF is typically managed by a combination of anti-arrhythmic drugs and external or internal electrical cardioversion. In addition, surgical compartmentalization or radiofrequency ablation of atrial tissue can be used. Unfortunately, long term success rates are low; AF recurrence is high with both drug treatment and electrical cardioversion with internal and external shocks.

Internal electrical cardioversion of AF remains an uncomfortable therapy option for managing patients with AF. Even with recent advancements, shock voltages necessary to defibrillate the atrial, while considerably lower than that for the ventricles, are still beyond the pain threshhold. One reason high voltages may be necessary is that the main generator for AF is the left atrium and direct access to the left atrium is problematic because of the risk of embolism. Typically, atrial defibrillation lead locations are limited to right sided chambers (right atrium and right ventricle) and venous structures accessible from the right side of the heart (coronary sinus).

To creat a trans-atrial shocking vector, the most common approach is to shock between one or more electrodes on the right side of the heart (right atrial appendage, superior vena cava, or right ventricle) to an electrode on the left side of the heart in the distal coronary sinus. The left atrium is also an important atrial chamber to defibrillate since *(i)* it can fibrillate independent of the right atrium, *(ii)* mapping studies have shown that earliestsites of activation following failed defibrillation arise from the left atrium for most defibrillation electrode configurations, *(iii)* early sites in or near the pulmonary veins have been shown to be responsible for the initiation of and early reoccurence of AF in many patients, and *(iv)* ablation of right atrial structures alone has had poor success in terminating AF or preventing its reoccurence. Nevertheless, there remains a need for means of defibrillating the atria of a subject without unduly high energy defibrillation pulses that would be painful to the subject being treated.

Summary of the Invention

A first aspect of the present invention is an implantable system for the defibrillation of the atria of a patient's heart. The system comprises *(a)* a first catheter configured for insertion into the right atrium of the heart, preferably without extending into the right ventricle of the heart; a first atrial defibrillation electrode carried by the first catheter and positioned at the atrial septum of the heart (*i.e.*, an atrial septum electrode); *(b)* a second atrial defibrillation electrode which together with the first atrial defibrillation electrode provides a pair of atrial defibrillation electrodes that are configured for orientation in or about the patient's heart to effect atrial defibrillation, and *(c)* a pulse generator operatively associated with the pair of

atrial defibrillation electrodes for delivering a first atrial defibrillation pulse to the heart of the patient. The second electrode may be configured for positioning through the coronary sinus ostium and in the coronary sinus or a vein on the surface of the left ventricle, such as the great vein. As explained further below, an additional electrode configured for positioning in the superior vena cava, right atrium (including the right atrial appendage, or the right ventricle may also be included, and the pulse generator may be configured or programmed for concurrently delivering a first defibrillation pulse through the additional electrode and the atrial septum electrode, and a second defibrillation pulse through the atrial septum electrode and the second electrode.

A second aspect of the present invention is a catheter assembly useful for the defibrillation or cardioversion of a patient's heart. The assembly comprises: *(a)* a first transveneous catheter configured for insertion into the heart of the patient, the first transvenous catheter having a proximal end portion, a distal end portion, and an elongate intermediate portion therebetween, and with the first transveneous catheter having a first electrode connected thereto; *(b)* a second transveneous catheter configured for insertion into the heart of the patient, the second transveneous catheter having a proximal end portion, a distal end portion, and an elongate intermediate portion therebetween; and *(c)* a connecting member attached to the first transveneous catheter, with the connecting member connected to the second transveneous catheter intermediate portion.

A further aspect of the present invention is a method for the defibrillation or cardioversion of the heart of a patient in need thereof while minimizing or reducing the voltage of the defibrillation pulses to be delivered. The method comprises the steps of: *(a)* positioning first and second defibrillation electrodes in operable association with the heart of the subject, the first and second defibrillation electrodes defining a gradient field in the heart, the gradient field including a region of the heart to be defibrillated; *(b)* positioning a third electrode in the gradient field between the first and second electrodes; and then *(c)* concurrently delivering *(i)* a first defibrillation pulse between the first and third electrode and *(ii)* a second defibrillation pulse between the second and third electrodes; with the first and second defibrillation pulses together effective to defibrillate the heart. The voltage required for each of the first and second defibrillation pulses is preferably less than the voltage necessary for a single defibrillation pulse delivered between the first and second electrodes that is

effective to defibrillate the heart. One, two or three or more additional electrodes may be positioned between the first, second and third electrodes to further reduce the voltage required, with additional shocks being delivered concurrently between various combinations of the electrodes (typically between adjacent electrodes).

A further aspect of the present invention is an implantable system for the defibrillation or cardioversion of a patient's heart. The system comprises: *(a)* first and second defibrillation electrodes configured for positioning in operable association with the heart of the subject, the first and second defibrillation electrodes when so positioned defining a gradient field in the heart between the first and second electrodes and in a region to be defibrillated; *(b)* a third defibrillation electrode configured for positioning in the gradient field between the first and second electrodes; and *(c)* a pulse generator operatively associated with the first, second and third defibrillation electrodes and configured for concurrently delivering *(a)* a first defibrillation pulse between the first and third electrode and *(b)* a second defibrillation pulse between the second and third electrodes. The two pulses are together effective to defibrillate the heart. Preferably, the voltage required for each of the first and second defibrillation pulses is less than the voltage required for a single defibrillation pulse delivered between the first and second electrodes that is effective to defibrillate the heart. Such an apparatus may be configured to carry out the methods described above.

In preferred embodiments of the foregoing methods and systems, there is further provided first and second transveneous catheters, wherein the first, second and third electrodes are carried by the first and second transveneous catheters, and wherein the first transveneous catheter is fixed to the second transveneous catheter.

In particularly preferred embodiments of the foregoing methods and systems, the first and second electrodes are carried by a first transveneous catheter, the first transveneous catheter having a proximal end portion, a distal end portion, and an elongate intermediate portion therebetween. The third electrode is carried by a second transveneous catheter, the second transveneous catheter having a proximal end portion, a distal end portion, and an elongate intermediate portion therebetween. The second transveneous catheter distal end portion is connected to the first transveneous catheter intermediate portion through a connecting member, as described in

connection with catheter assemblies above. The third electrode is then, preferably, an atrial septum electrode.

The foregoing and other objects and aspects of the present invention are explained in greater detail in the drawings herein and the specification set forth below.

Brief Description of the Drawings

Figure 1 illustrates a first embodiment of an implantable system of the present invention, in which the atrial septum electrode is a trans-septal electrode. The heart is shown in partial cut-away view, with the right atrium, the right ventricle, and a portion of the left atrium being shown in cross section. The surface of the left ventricle is shown so that vessels on the surface of the ventricle that are accessed through the coronary sinus (shown in dashed lines) may be seen.

Figure 2 illustrates a second embodiment of an implantable system of the present invention, in which the atrial septum electrode is fixed to the atrial septum by means of a terminal screw.

Figure 3 illustrates a third embodiment of an implantable system of the present invention, in which the atrial septum electrode is incorporated into an expandable umbrella device which is opened within the right atrium to hold the electrode against the atrial septum.

Figure 4 illustrates a fourth embodiment of an implantable system of the present invention, in which the atrial septum electrode is fixed to the coronary sinus electrode to form a catheter assembly and facilitate the holding of the atrial septum electrode against the atrial septum.

Figure 5 illustrates a catheter assembly as used in Figure 4, in which the first catheter is permanently fixed to the second catheter.

Figure 6 illustrates an alternate embodiment of a catheter assembly of the present invention, in which the first catheter is releasably fixed to the second catheter by means of a retractable loop.

Figure 7 illustrates a further alternate embodiment of a catheter assembly of the present invention, in which the first catheter is releasably fixed to the second catheter by means of an elastic loop.

Figure 8 illustrates a still further alternate embodiment of a catheter assembly of the present invention, in which the connecting member is positioned on an intermediate portion rather than the distal portion of the first catheter.

Figure 9 illustrates a still further alternate embodiment of an implantable system incorporating a catheter assembly of the present invention, in which the second catheter extends into the right ventricle and is fixed to the apex of the right ventricle by means of a terminal screw.

Figure 10 illustrates a further embodiment of a catheter assembly of the present invention, in which the second catheter includes an expandable stent to further anchor the second catheter within a suitable vessel, such as a pulmonary artery.

Figures 11A-C schematically illustrate a technique for lowering shock voltage that may be used in conjunction with the instant invention or other defibrillation techniques.

Figure 12 schematically illustrates a technique for lowering ventricular defibrillation voltage that implements the technique illustrated in Figures 11A-C.

Figure 13 shows the ADFT leading edge voltage in experimental animals used to demonstrate the instant invention.. The leading edge voltage of configuration A2 is significantly lower than the others (number shows the percent lower).

Figure 14 shows the ADFT leading edge current in experimental animals used to demonstrate the instant invention. The leading edge current of configuration A2 is significantly lower than the others (number shows the percent lower).

Figure 15 shows the ADFT total shock energy in experimental animals used to demonstrate the instant invention. The shock energy of configuration A2 is significantly lower than the others (number shows the percent lower).

Detailed Description of the Preferred Embodiments

The present invention is explained in greater detail below. This description is not intended to be a detailed catalog of all the different ways in which the invention may be implemented, or all the features that may be added to the instant invention. For example, features illustrated with respect to one embodiment may be incorporated into other embodiments, and features illustrated with respect to a particular embodiment may be deleted from that embodiment. In addition, numerous variations and additions to the various embodiments suggested herein will be apparent to those

skilled in the art in light of the instant disclosure which do not depart from the instant invention. Hence, the following specification is intended to illustrate some particular embodiments of the invention, and not to exhaustively specify all permutations, combinations and variations thereof.

The terms "atrial septum electrode" or electrode positioned "at the atrial septum", as used herein, refer to an electrode that is, or is configured to be, inserted through the atrial septum (*i.e.*, a trans-septal electrode), inserted into the atrial septum (*i.e.*, inserted partially into the septum without penetrating completely through the septum), or substantially contacted to the surface of the atrial septum (typically the surface facing the right atrium). An atrial septum electrode may also be an electrode that is directly or indirectly secured to the atrial septum, but is spaced up to about 1, 2, or 4 millimeters or more away from the septum, where the electric field produced from the electrode is effective in stimulating the atrial septum in substantially the same manner as an electrode inserted into or contacting to the atrial septum. Patients treated by the methods of the present invention are typically human.

The term "catheter" is used interchangeably with "lead" herein, and is not meant to imply that the particular structure has an interior lumen for receiving a guide wire or the like, as such a lumen is optional in carrying out the present invention, and the use of one or more guidewires is optional in carrying out the present invention.

The term "concurrently", when used herein with respect to two or more defibrillation pulses, refers to pulses that are administered sufficiently close in time so that the combined therapeutic effect is greater than the sum of the therapeutic effects when the pulses are administered singly. Such pulses may be administered simultaneously, partially overlapping in time, or sequentially in time. When administered sequentially in time the pulses may or may not have an intervening time period therebetween. Preferably, the onset of a subsequent pulse occurs within 100, 200 or 500 milliseconds of the offset of a preceding pulse.

The term "defibrillation pulse" is used herein to encompass any of a variety of defibrillation, or cardioversion, waveforms. The particular type of pulse delivered is not critical and may, for example, comprise: a monophasic or biphasic waveform; a pulse that includes a series of waveforms; waveforms that are uniform, stepped, saw-toothed, truncated exponential, *etc.*

The term "pulse generator" as used herein is intended to encompass any type of device, preferably contained within an implantable housing to form an implantable cardioverter defibrillator (ICD), that delivers the defibrillation pulse or pulses desired to achieve a particular method. In general, such pulse generators comprise a battery power supply, a control circuit, and a capacitor (or capacitor circuit). The control circuit is connected to the battery and the capacitor for charging the capacitor and delivering a therapeutic defibrillation pulse from the capacitor through the defibrillation electrodes. The control circuit typically includes a detection circuit for monitoring the heart of a subject and determining when the capacitor should be charged and a therapeutic pulse delivered. Numerous additional features may be included, as is known to those skilled in the art.

A. Atrial septum electrodes for atrial defibrillation.

As noted above, the present invention provides an implantable system for the defibrillation of the atria of a patient's heart. Such a system typically comprises a first catheter configured for insertion into the right atrium of the heart; a first atrial defibrillation electrode carried by the first catheter and positioned at the atrial septum of the heart; a second atrial defibrillation electrode which together with the first atrial defibrillation electrode provides a pair of atrial defibrillation electrodes that are configured for orientation in or about the patient's heart to effect atrial defibrillation, and a pulse generator operatively associated with the pair of atrial defibrillation electrodes for delivering a first atrial defibrillation pulse to the heart of the patient. It will be appreciated that the atrial septum electrode need not be used in conjunction with every pulse or shock delivered by the system and methods as long as it used in some of the pulses or shocks delivered by the system and methods.

Figure 1 illustrates a first embodiment of an implantable system of the present invention. The heart **20** is shown in partial cut-away view, with the right atrium **21**, the right ventricle **22**, and a portion of the left atrium **23** being shown in cross section. The surface of the left ventricle **24** is shown so that veins or vessels **25** on the surface of the ventricle that are accessed through the coronary sinus **26** (shown in dashed lines) and the coronary sinus ostium **27** may be seen. A pair of catheters **30, 31,** enter the heart through the superior vena cava **28.** One catheter is positioned through a trans-septal puncture formed in the atrial septum so that the atrial septal electrode **32**

that is connected to that catheter extends through the septum. An introducer sheath, needle, or the like may be used to form the puncture and introduce the electrode therethrough, as will be apparent to those skilled in the art. The other catheter extends through the ostium of the coronary sinus and through the coronary sinus and into a vessel on the surface of the left ventricle of the heart (*e.g.,* the great vein), where an additional defibrillation electrode **33** connected to that catheter is positioned.

The system includes an implantable cardioverter defibrillator (ICD) **40** comprises a housing **41** containing a pulse generator **42,** with a subcutaneous electrode **43** located on the external surface of the housing as described in U.S. Patent No. 5,292,338 to Bardy. The defibrillator is then implanted in the left or right (preferably left) thoracic region of the patient (*e.g.,*subcutaneously, in the left pectoral region, in accordance with known techniques. The housing electrode **43** may be used in conjunction with or in alternative to other catheter mounted electrodes.

Sensing of atrial fibrillation for triggering of a defibrillation can be carried out through any suitable means, and may employ the same electrodes that are used for defibrillation or separate sensing electrodes. In the alternative, the defibrillation pulse may, if desired, be triggered manually or externally by an operator or the patient. It will be appreciated that a sensing electrode (not shown) will also preferably be provided in the right ventricle, *e.g.* on a separate catheter, to sense the ventricular cycles and deliver this information to the pulse generator so that the pulse generator delivers the atrial defibrillation pulse or pulses at a time when ventricular fibrillation is not likely to be induced thereby, as is known in the art.

While the atrial septum electrode is primarily described herein for the delivery of atrial defibrillation or cardioversion pulses, it will be appreciated that the system can be configured to carry out other useful methods from the atrial septum electrode. For example, an atrial septum electrode can be used to deliver pacing pulses from the pulse generator prior to the onset of atrial fibrillation to reduce the chance of atrial fibrillation occuring. In addition, an atrial septum electrode can be used to deliver pacing pulses after the onset of atrial fibrillation, but before a defibrillation pulse is delivered, in an effort to avoid the need to deliver a defibrillation pulse. If fibrillation continues after the pacing pulse is delivered, then a defibrillation pulse can be delivered. The atrial septum electrode used to deliver such pacing pulses may be the

same or different from the atrial septum electrode used to deliver defibrillation pulses (*e.g.*, multiple adjacent atrial septum electrodes may be provided on a single catheter).

Figure 2 illustrates a second embodiment of an implantable system of the present invention. This system again comprises a pair of an implantable ICD **50**, a pair of catheters **51, 52,** an atrial septum defibrillation electrode **54**, and an additional defibrillation electrode **55** in the great vein. The atrial septum electrode is fixed to the atrial septum by a terminal screw or helix **56** connected to the distal end portion of catheter **51,** which penetrates partially into (or all the way through) the atrial septum. Of course, any suitable connecting means may be employed in addition to a terminal screw or helix, including but not limited to a retractable hook connected to the distal end portion of the catheter **51.**

Figure 3 illustrates a third embodiment of an implantable system of the present invention, again including an implantable ICD **70,** a pair of catheters **71, 72,** and a defibrillation electrode **73** positioned in the great vein. The atrial septum electrode **74** is incorporated into an expandable device or element **75** which is opened within the right atrium (or allowed to open within the atrium by removal of an introducer sheath or the like) to hold the electrode **76** against the atrial septum by expanding to a size about the same as or slightly greater than the interior diameter of the right atrium and forcing the electrode against the atrial septum . In the alternative, an expandable element could be used in conjunction with a helix, screw, hook or other fixing means located on the distal tip of the catheter to unfold the electrode into a configuration contacting the atrial septum, to thereby provide better contact or expanded contact area of the defibrillation electrode against the atrial septum.

Figure 4 illustrates a particularly preferred embodiment of an implantable system of the present invention, in which the catheter **90** carrying the atrial septum electrode **91** is fixed to the catheter **92** carrying coronary sinus electrode **93** to form a catheter assembly and facilitate the holding of the atrial septum electrode against the atrial septum. The system includes an ICD **94,** which again may incorporate features such as described in connection with ICDs as set forth above. A connecting member **95**, typically located at the distal end portion of the first catheter and connected to the intermediate portion of the second catheter, is included for interconnecting the two catheters. Such a configuration or assembly, in addition to being particularly suitable

for carrying out the present invention has a variety of different applications, and is discussed in greater detail in section B below.

B. Catheter assembly with fixation of one catheter to another.

The present invention provides a catheter assembly useful for the defibrillation or cardioversion of a patient's heart, of which the assembly illustrated in **Figure 4** is one example. As noted above, such assemblies typically comprise a first transveneous catheter configured for insertion into the heart of the patient, the first transvenous catheter having a proximal end portion, a distal end portion, and an elongate intermediate portion therebetween. The first transveneous catheter typically has a first electrode connected thereto. The first electrode is typically connected to the first transveneous catheter intermediate portion, although it will be noted that the intermediate portion is quite elongate and the first electrode may be positioned anywhere along the length thereof.

A second transveneous catheter configured for insertion into the heart of the patient is also included in the assembly, the second transveneous catheter also having a proximal end portion, a distal end portion, and an elongate intermediate portion therebetween. The second catheter may, for example, be configured for positioning in a suitable location, such as into the right ventricle, optionally extending to the apex of the right ventricle, through the ostium of the coronary sinus and into or through the coronary sinus, *etc.* The assembly further includes a connecting member attached to the first transveneous catheter (*e.g.*, at the distal end portion or at the proximal portion thereof), with the connecting member connected to the second transveneous catheter intermediate portion.

The second transveneous catheter generally has at least one electrode connected thereto (*.e.g.*, an electrode for positioning in the coronary sinus or a vein on the surface of the left ventricle), which electrode may be a therapeutic, or defibrillation, electrode, and/or a monitoring electrode such as a ring electrode or tip electrode. However, the second transveneous catheter need not necessarily carry an electrode if it functions primarily to secure or anchor the first catheter in place. Hence, the second catheter may be referred to as an "anchoring catheter" or "positioning catheter".

While such catheter assemblies may be used for atrial defibrillation systems and methods as described herein, it is also envisioned that such catheter assemblies will find a variety of additional applications, such as for ventricular defibrillation or cardioiversion, whenever it is desirable to securely fix a particular catheter in place.

Figure 5 illustrates a catheter assembly **110** of the present invention, which may be configured in any suitable manner including but not limited to that shown in **Figure 4**. The assembly comprises a first catheter **111** having a proximal end portion, **112**, a distal end portion **113**, and an elongate intermediate portion **114** therebetween. Note that proximal end portions will typically terminate in a connector (not shown) to facilitate mechanical connection of the catheters to the ICD and electrical connection of the electrodes to the pulse generator contained therein. A first defibrillation electrode **115** is connected to the intermediate portion **114.** A connecting member **116** is connected to the distal end portion **113** of the first catheter, and is permanently fixed to the second catheter **118** (*e.g.*, by permanently fastening two separate members; by integrally forming the two members together). Second catheter **118** also has a proximal end portion **119**, a distal end portion **120**, and an intermediate portion **121**, with a defibrillation electrode **122** positioned proximal to the connecting member and a further defibrillation electrode **123** positioned distal to the connecting member. As noted above, either or both of the electrodes on the second catheter are optional, and additional electrodes such as sensing electrodes could be included if desired.

Figure 6 illustrates an alternate embodiment of a catheter assembly **130** of the present invention, in which the first catheter **131** is releasably fixed to second catheter **132** by means of a retractable loop **133**. Any suitable means can be used to retract the loop, such as the insertion of a tendon **134** through a lumen in catheter **131** which connects to the loop, and which can be drawn back to tighten the loop. As with any other such releasably secured connecting member, the loop can be fastened around an intermediate portion **135** of the catheter assembly at any of a variety of locations to optimally configure the electrode assembly for a particular patient. The intermediate portion **135** can be substantially smooth as illustrated, or may be textured or the like to enhance fastening of the loop to the catheter and reduce lateral slippage along the length of the second catheter intermediate portion. If desired, an introducer sheath (not shown) can be deployed around the second catheter and used to push the loop forward down the second catheter until the desired location is achieved (*e.g.*, just

outside or proximal to the coronary sinus ostium, when the second catheter is inserted through the ostium), with the loop then being tightened and the introducer sheath removed. In the alternative, an introducer can be used to carry the second catheter to the desired position rather than push the connecting member to the desired position.

Figure 7 illustrates a further alternate embodiment of a catheter assembly **150** of the present invention, in which the first catheter **151** is releasably fixed to the second catheter **152** by means of an elastic loop **153**. The elastic loop may be formed of any suitable polymeric material, metallic material or the like that is sufficiently resilient to allow its deformation and reformation around the second catheter (and, if necessary, around the first catheter). The distal end portion **154** of the first catheter is enlarged to reduce the chance of the resilient loop slipping off the tip thereof (or, in the alternative or in addition thereto, the resilient loop could be permanently fastened to the first catheter). As in the embodiment of **Figure 6**, an introducer sheath may be deployed around the second catheter to push the elastic loop to the proper location around the second catheter. Again, texturing or the like could be provided on the intermediate portion of the second catheter to reduce slippage along the length thereof.

In a variation to the embodiment described above in connection with **Figure 7**, the fastening loop **153** could be substantially inelastic, if the second and/or first catheter itself were sufficiently elastic to allow the catheter to be forced therethrough, yet sufficiently resilient to secure the catheters to the loop when forced to the desired location by means of an introducer sheath or the like.

Figure 8 illustrates a still further embodiment of a catheter assembly **170** of the present invention, in which the connecting member (a retractable loop **171** with a tendon **172** as illustrated) is positioned on an intermediate portion **173** of the first catheter **174** rather than the distal portion of the first catheter as shown above. Any number of electrodes could be included in such an embodiment. As illustrated, the first catheter **174** has electrodes **175, 176** proximal and distal to the connector, and the second catheter **178** has electrodes **180, 181** proximal and distal to the loop connector. Such an assembly could be used, for example, to position electrode **180** in or through the coronary sinus, electrode **176** in the right ventricle, electrode **175** at the atrial septum, and electrode **181** in the right atrium or superior vena cava.

Figure 9 illustrates a still further alternate embodiment of an implantable system comprising an ICD **190**, and a pair of catheters **191, 192** configured as an assembly through a connector **193.** Here the second catheter extends into the right ventricle and is fixed to the apex of the right ventricle by means of a terminal screw or helix **194**. Any other terminal fastening means, such as a retractable hook, could also be employed.

Figure 10 illustrates a further embodiment of a catheter assembly **210** of the present invention, comprising first and second catheters **211, 212**, and in which the second catheter includes an expandable stent **213** that is expanded or retracted by tendon **214** to further anchor the second catheter within a suitable vessel, such as a pulmonary artery. Such an additional anchoring feature could be added as appropriate to any of the embodiments described above.

C. Location of additional electrodes to lower shock voltage and energy required for defibrillation.

A further aspect of the present invention is a method for the defibrillation or cardioversion of the heart of a patient in need thereof while minimizing the voltage of defibrillation pulses to be delivered. As noted above, the method involves, first, positioning first and second defibrillation electrodes in operable association with the heart of the subject, the first and second defibrillation electrodes defining a gradient field in the heart, the gradient field including a region of the heart to be defibrillated. Next, a third electrode (*e.g.,* an atrial septum electrode) is positioned in the gradient field between the first and second electrodes. Then, a first defibrillation pulse between the first and third electrode and a second defibrillation pulse between the second and third electrodes are concurrently delivered, with the first and second defibrillation pulses together effective to defibrillate the heart. The voltage required for each of the first and second defibrillation pulses is preferably less than the voltage necessary for a single defibrillation pulse delivered between the first and second electrodes that is effective to defibrillate the heart. All of the electrodes may be carried on transveneous catheters, either separately or with multiple electrodes on a single catheter.

Such a technique can be used for any of a variety of purposes, including treating patients afflicted with atrial fibrillation and patients afflicted with ventricular

fibrillation. For atrial fibrillation, each of the first and second defibrillation pulses are preferably not greater than, and more preferably less than, 50, 100, or 150 volts in magnitude, and each of the first and second defibrillation pulses are preferably not greater than, and more preferably less than, one, two or four Joules in magnitude. Preferably, the gradient field created by the first defibrillation pulse and the second defibrillation pulse in the region of the heart to be defibrillated is at least 3 or 4 volts per centimeter. The specific minimum potential gradient (which must be created throughout all, or substantially all, of the fibrillating myocardium), differs for different defibrillation waveforms, but is thought to be in the range of approximatley 4 to 7 volts per centimeter, with at least about a 4 volt per centimeter gradient needed for a good biphasic defibrillation waveform.

Figures 11A-C schematically illustrates such a technique. Panel A illustrates an original pair of electrodes (A and B) that create a substantially even potential gradient field in the region between the two electrodes, with the gradient field including a region in the atria or ventricles or the heart of a patient to be defibrillated. Assuming that (1) the electrodes are 20 cm apart, (2) the conductivity of the medium is substantially uniform, and (3) there is no substantial voltage loss at the electrode-media interface, and (4) a 4 volt per centimeter potential gradient must be created throughout the region, then a shock voltage of about 80 volts will be required. Panel B shows a third electrode (**C**) approximately half way between the original pair of electrodes (**A,B**). A shock between electrodes A and C will create a potential gradient of 4 volts per centimeter in the left half of the region with a 40 volt shock. Similarly, a 40 volt shock between electrodes C and B will create the desired 4 volt per centimeter potential gradient throughout the right half of the region. If the two shocks are given concurrently and are substantially the same duration as the original shock through electrodes A and B, then the voltage of each shock will be approximately half that of the original, while the total energy of the two shocks will be the same as that of the original shock. Therefore, the maximum voltage delivered to the heart of the patient in this example will be about 40 volts rather than 80 volts.

More than three electrodes may be used to implement this technique. For example, panel **C** of **Figure 11** shows the addition of two additional electrodes (**D** and **E**). Concurrent (*e.g.*, sequential) shocks through four pairs of electrodes (A to D, D to

C, C to E, and E to B) in various sequences will again reduce the voltage in half to 20 volts while maintaining the same total energy.

When this technique is used for atrial defibrillation, such as with a system and/or catheter assembly as illustrated in connection with Figures 1-10 above, the method may comprise the steps of: *(a)* positioning a first defibrillation electrode in the right atrium (including the right atrial appendage), superior vena cava or right ventricle of the subject; *(b)* positioning a second defibrillation electrode in the coronary sinus or a vein on the surface of the left ventricle of the heart (*e.g.*, the great vein); *(c)* positioning a third electrode at the atrial septum of the heart; and then *(d)* concurrently delivering *(i)* a first defibrillation pulse between the first and third electrode and *(ii)* a second defibrillation pulse between the second and third electrodes. Preferably, each of the first and second defibrillation pulses has an energy not greater than, or less than, one, two or four Joules, preferably each of the first and second defibrillation pulses has a voltage less than 50, 100 or 150 volts, preferably the first and second defibrillation pulses are delivered within 500 milliseconds of each other, and preferably the gradient field created by each defibrillation pulse in the heart of the patient is greater than 4 volts per centimeter.

The foregoing method of reducing shock voltage may be implemented in techniques other than atrial defibrillation. For example, **Figure 12** schematically illustrates a technique for lowering ventricular defibrillation threshholds during open-chest cardiac surgery with an array of three or more epicardial electrodes. The particular electrode array of Figure 12 is similar to the array of Figure 11C. Such a system decreases the voltage needed for defibrillation in the operating room, which could decrease the damaging effects associated with large defibrillation shocks. Since the electrodes in Figure 12 are placed on the epicardium, they will not have as much effect on the shock potential gradient field in the ventricular septum as they will in the ventricular free walls. A modification of this system to increase the potential gradient in the septum is, accordingly, to add an additional electrode (F) place in the right ventricular cavity against the inter-ventricular septum, optionally as part of a catheter. Then, in addition to the various possible concurrent shock sequences through electrodes A to E, one or more shocks could be delivered from electrode F to some or all of electrodes A to E. Systems for implementing such methods can be provided with the necessary electrodes operably associated with a pulse generator configured or

programmed to carry out the shock patterns described herein in accordance with known techniques.

The present invention may be implemented in combination with, or employing the features of, numerous additional methods and systems for the defibrillation and cardioversion of a patient's heart, including but not limited to those disclosed in U.S. Patent No. 6,006,131 to Cooper et al.; U.S. Patent No. 6,002,962 to Huang et al.; U.S. Patent No. 5,987,354 to Cooper et al.; U.S. Patent No. 5,978,705 to Ideker et al.; U.S. Patent No. 5,978,704 to Ideker et al. U.S. Patent No. 5,509,925 to Adams; U.S. Patent No. 5,630,834 to Bardy; and U.S. Patent No. 5,476,499 to Hirschberg. The disclosures of all U.S. Patent references cited herein are to be incorporated herein by reference in their entirety.

The present invention is further illustrated in the experimental examples set forth below.

EXAMPLES

Reduction of Atrial Defibrillation Threshold With an Interatrial Septal Electrode

This example demonstrates that an electrode configuration with an interatrial septal electrode placed approximately midway between the right atrial appendage and coronary sinus electrodes increases the potential gradient in this region and thus lowers the atrial defibrillation threshold (ADFT).

I. METHODS

All studies were performed in accordance with the guidelines established in the Position of the American Heart Association on Research Animal Use adopted by the American Heart Association on November 11, 1984.

Of 11 adult sheep, 8 (41±6 kg, heart mass 217±8 g) completed the experimental protocol; only data from these 8 animals were compiled.

Animal Preparation. As a preanesthetic agent, a 1-to-1 mixture of tiletamine and zolazepam (8-10 mg/kg) was given intramuscularly. About 10 minutes later, thiopental (2-6 mg/kg) was administered as a slow intravenous bolus. The animal was laid in a dorsally recumbent position on a fluoroscopy table, intubated, and placed on a volume-cycled ventilator (tidal volume: 15-20 ml/kg) with a 4% isoflurane/oxygen

mixture at a rate of 8-12 breaths per minute. The isoflurane concentration was decreased to 1.5-3.5% to maintain a deep surgical plane of anesthesia. Ventilator settings were adjusted as necessary to correct for respiratory acidosis or hypoxemia. Intravenous fluids (Lactated Ringer's solution) were infused throughout the experiment with supplemental electrolytes as needed as determined by serial blood gas and chemistry analyses conducted every 30-60 minutes.

An 8 Fr. sheath was placed in the left femoral artery percutaneously for continuous arterial pressure monitoring. The animal was instrumented for lead II ECG and esophageal temperature monitoring. A heated water blanket was used to maintain body temperature at 37±1°C. Neuromuscular blockade was achieved with a 1 mg/kg succinylcholine chloride intravenous bolus followed by an intravenous drip (5-8 mg/min) for maintenance, depending upon neuromuscular tone. At all times, an external defibrillator with external paddles was available in the event of non-perfusing ventricular tachyarrhythmia.

Defibrillation Catheter Placement. All catheters were positioned transvenously under fluoroscopic guidance. Through a jugular vein, a defibrillation lead (Perimeter #7109, Guidant Corp., St. Paul, MN) with a distal 6-cm long electrode was situated with its coil electrode in the distal coronary sinus (CS) along the left lateral heart and its tip under the left atrial appendage. Care was taken to not place this lead in the persistent superior vena cava, which is present in this species. A modified quadripolar catheter (Mansfield EP-Boston Scientific Corp., Watertown, MA) with a 3.5-cm-long coil electrode 1 cm proximal to the catheter tip was positioned in the right atrial appendage (RAA) through the left femoral vein. The coil electrode was laid along the superior wall of the RAA. The bipolar tip of this catheter was used for the burst-pacing induction of AF. Another two 3.5-cm-long coil electrode catheters were also placed in the main and left pulmonary artery (PA) and lower right atrium (LRA), respectively. The LRA electrode was positioned at the junction of right atrium and inferior vena cava.

A custom-made 6-cm coil electrode that served as the interatrial septal electrode (SP) was constructed along a catheter; the distal end of the electrode was 3 cm from the catheter tip. It was situated through a trans-septal procedure. An 8 Fr. Mullins sheath was advanced into the right atrium through the right femoral vein over a 0.038" guide wire. Then, a Brockenbrough needle replaced the guide wire and was

displaced through the atrial septum, usually under LAO projection. Confirmation of left atrial catheterization was made by measurement of oxygen saturation of blood withdrawn through the Brockenbrough needle and with contrast injection into the left atrium during fluoroscopy. A stiff 0.038" guide wire was positioned in the left atrium through the sheath. The Mullins sheath was then withdrawn over the wire, leaving the wire in the left atrium. Next, an 11 Fr. guide sheath was advanced over the wire and into the left atrium. After withdrawal of the dilator and guide wire, the septal electrode was inserted into the left atrium through the guide sheath. The tip of the septal electrode catheter was placed against the lateral wall of left atrial appendage. About 2/3 of the electrode was in the left atrium and 1/3 in the right atrium. After the septal electrode was in position, 1000 units of heparin were given intravenously every hour.

Additionally, a three-electrode defibrillation catheter (Endotak DSP, Guidant Corp., St. Paul, MN) was introduced into the right ventricle through the other jugular vein; the two lead-body coil electrodes from this catheter were situated in the right ventricle (RV) and superior vena cava (SVC). The tip electrode from this catheter was used for ventricular pacing. A three-wire subcutaneous array (SQA) was inserted over the left side of the heart. In the event of ventricular tachyarrhythmias, the electrode configuration for ventricular defibrillation was RV as the first phase anode with CS, SVC and SQA electrically common as the first phase cathode (RV $\rightarrow$ CS+SVC+SQA).

Induction of Atrial Fibrillation. To allow AF to be maintained, acetyl-β-methylcholine chloride (Sigma Chemicals Co., St Louis, MO) was continuously infused into the pericardium. The pericardial space was approached percutaneously under fluoroscopic guidance with a 3-inch-long 16-gauge needle from just inferior to the right subxiphoid position with the animal turned about 20 degrees toward the right side. When the needle was confirmed to be within the pericardial space by contrast injection, a guide wire was gently inserted within the needle into the pericardial space. The pericardial location for the guide wire was confirmed by inability to move it outside the fluoroscopic image of the heart silhouette. After removal of the needle, a 6 Fr. sheath was advanced into the pericardial space over the wire. After flushing with acetyl-β-methylcholine chloride, a 4 Fr. pig-tail catheter was inserted through the

sheath. Typically, the catheter tip was advanced to near the left atrial appendage and the sheath was removed.

Acetyl-β-methylcholine chloride solution (1 g / 250 ml saline) was infused at a rate of 20 μL/min using a micro-infuser. Burst pacing used to induce AF consisted of 2-ms stimuli delivered at intervals of 30-60 ms. AF was defined as irregular rapid atrial activity with an irregular ventricular response on the ECG. Blood pressure and heart rate were recorded before and 20 min after acetyl-β-methylcholine infusion

Defibrillation Waveforms and Lead Configurations. Once acetyl-β-methylcholine chloride was infused long enough to support AF maintenance of >10 minutes (typically ~20 minutes), the defibrillation protocol was begun. The waveform generation system has been described previously (R. Cooper et al., *Circulation*. 1997;96:2693-2700). Briefly, a monophasic waveform was produced by a programmable defibrillator (HVS-02, Ventritex, Inc). This monophasic waveform was divided into a biphasic, truncated-exponential waveform by a high-voltage, cross-point switch; for sequential shocks, two biphasic, truncated-exponential waveforms were created with the use of an additional pair of cross-point switches. Each biphasic waveform had a first-phase duration of 3 ms and a second-phase duration of 1 ms. The interval between each phase of the biphasic waveforms and between the two biphasic waveforms of sequential shocks was 20 μsec. Because all stimuli (single or sequential shocks) were produced from the output of one defibrillator, all phases of the waveforms exhibited decaying voltage from a single capacitor, in which the trailing-edge voltage of each preceding phase was equal to the leading-edge voltage of the succeeding phase.

In each animal, the ADFTs of five test configurations were determined (**Table 1**). Three configurations utilizing the septal electrode were named A1, A2 and A3. The two others were named B and C, respectively. The order of determining the test-configuration ADFTs was randomized in each animal as follows. The order among A, B and C was initially randomized, and then the order of A1, A2 and A3 (within A) was randomized. The ADFTs of the configurations utilizing the septal electrode were measured consecutively in order to obviate the need for repositioning this electrode. During the ADFT testing of any configuration, passive electrodes not delivering any shock for that configuration were removed. To minimize the likelihood of ventricular tachyarrhythmia induction, shock delivery was synchronized to right-ventricular

pacing, which triggered the Ventritex defibrillator and cross-point switches via custom software on a Macintosh Computer. The cycle length of this pacing was 250-400 ms, depending on the ventricular rate during AF. Shocks were delivered 20 ms after the 8th pacing pulse.

Table 1. Test Configurations

	First Shock		Second Shock		Biphasic
	Anode	Cathode	Anode	Cathode	Waveform
A1	RAA+CS	SP			Single
A2	RAA	SP	CS	SP	Sequential
A3	CS	SP	RAA	SP	Sequential
B	RAA	CS			Single
C	RAA	CS	LRA	PA	Sequential

RAA: right atrial appendage, CS: coronary sinus, SP: atrial septum, LRA: low right atrium, PA: pulmonary artery.

The ADFT of each test configuration was determined using a multiple-reversal method with an initial starting peak voltage of 100 V and step sizes of 40/20/10 V. If the initial shock failed, the next and subsequent shock voltages were increased by 40 V until a shock succeeded. Following the first shock that successfully terminated AF, the voltages of subsequent shocks were decreased by 20 V until a shock failed. Then the shock voltages were increased by 10 V until a shock succeeded again. Conversely, if the initial shock succeeded, subsequent shock voltages were decreased by 40 V until a shock failed. Then shock voltages were increased by 20 V until a shock succeeded, after which shock voltages were decreased by 10 V until a shock failed again. The last successful shock of the third reversal was deemed the ADFT of the test configuration. Before starting the defibrillation protocol, 3-5 test shocks were given. All test shocks were delivered after inducing AF and allowing it to be sustained 1 minute. When a test shock failed, a rescue shock of 200-300 V was given. A 1-2 min period of sinus rhythm was allowed before the next induction of AF.

Data Acquisition. The leading-edge (peak) voltage and current of each test shock were recorded, and the impedance and delivered energy of each shock were computed by a waveform analyzer (DATA 6100, Data Precision).

Postmortem Examination. After the completion of data collection, euthanasia was induced with an intravenous bolus of potassium chloride. The chest was opened and the location of the electrodes of the last test configuration was

confirmed by palpation through the heart walls. The heart was then removed. The great vessels were trimmed to the point of insertion into each cardiac chamber, and the pericardium was removed. The mass of the heart was determined.

Statistical Analysis. Results are expressed as the mean±SD. The overall effect of the 5 test configurations on each ADFT characteristic was tested by repeated-measures ANOVA. Pair-wise differences in measures between the 5 configurations were tested by paired t tests. A value of $P< 0.05$ was considered significant.

II. RESULTS

Reproducible, sustained AF could be induced in all animals. The ventricular rate in sinus rhythm before and 20 min after administration of acetyl-β-methylcholine was similar (112±8 vs. 109±11 beat/min, respectively, P=NS). The drug significantly lowered the sinus-rhythm systolic/diastolic blood pressure, however (107±8/83±4 vs. 84±7/62±5 mmHg, $P<0.05$). During AF, the ventricular rate varied from 80 to 178 beat/min (131±36 beat/min). After successful test shocks, sinus rhythm usually recovered quickly (<1.5 sec). In 1 sheep with a long sinus recovery time (>2-4 sec), temporary post-shock atrial pacing was performed.

Leading Edge Voltage. The ADFT leading-edge-voltage of the 5 configurations is shown in **Figure 13**. The ADFT leading-edge-voltage of configuration A2 (RAA → SP / CS → SP; 71±16 V) was significantly lower than each of the other 4 configurations (A1: 102±36 V; A3: 121±34 V; B: 156±38 V; and C: 96±29 V). The ADFT leading-edge-voltage of configuration B (RAA → CS) was significantly higher than the other 4 configurations.

Leading Edge Current. The ADFT leading-edge-current is shown in **Figure 14.** The ADFT leading-edge-current of configuration A2 (1.68±0.48 A) was significantly lower than that of the other 4 configurations A1, A3, B and C (A1: 4.32±1.59 A; A3: 3.61±1.28 A; B: 2.99±1 A; and C: 1.92±0.65 A). The ADFT leading-edge-current of configuration C was lower than that of configurations A3 and B. The leading-edge-current ADFT of configuration A1, which was the sum of the currents of two pathways: RAA → SP and CS → SP, was higher than that of configurations A2, B and C but not configuration A3.

Impedance. The impedances of the test configurations are shown in **Table 2**. Impedances of the same pathway in different test configurations were not significantly different. Configuration A1 exhibited the lowest impedance, which was approximately the reciprocal of the sum of the reciprocal impedances of its two pathways (RAA → SP and CS → SP) as estimated from individual shocks across these pathways during sequential shocks.

Shock Energy. The ADFT shock-energy of the 5 configurations is shown in **Figure 15**. Configuration A2 had a significantly lower ADFT shock-energy than each of the other 4 test configurations (A2: 0.39±0.17 J vs. A1: 0.86±0.59 J, A3: 1.16±0.72 J, B: 1.27±0.67 J, and C: 0.68±0.46 J; $P<0.05$ for each comparison). The ADFT shock-energy of configuration A2 was lower than that of configurations A1, A3, B and C by 46±20%, 63±14%, 68±8%, and 36±15%, respectively. Configuration C had a lower ADFT shock-energy than configurations A1, A3 and B ($P<0.05$ for each comparison). Compared with configuration B, configuration C reduced shock energy by 50±9%. Configuration A1 had a lower ADFT shock-energy than configuration B (37±15% lower, $P<0.05$), but not than configuration A3. The difference in ADFT shock-energy between configurations A3 and B was not significant.

Table 2. Impedances of all the current pathways

	Current Pathways		Impedance(Ω)
A1	Single	RAA+CS → SP	25 ±3
A2	First	RAA → SP	46 ±3
	Second	CS → SP	34 ±4
A3	First	CS → SP	35 ±4
	Second	RAA → SP	45 ±4
B	Single	RAA → CS	54 ±6
C	First	RAA→ CS	54 ±7
	Second	LRA → PA	49 ±4

RAA: right atrial appendage, CS: coronary sinus, SP: atrial septum,
LRA: low right atrium, PA: pulmonary artery.

While care must be used in directly extrapolating the results of this study to humans because of the particular pharmaceutical interventions employed.

Nevertheless, this study demonstrates that, in an acute sheep model of sustained AF, atrial defibrillation configurations utilizing an additional electrode at the interatrial septum were more efficacious than the present standard configuration by which cardioversion is achieved with RAA → CS. The ADFT shock-energy of RAA+CS → SP was 37±15% lower, and sequential shock configuration RAA → SP / CS → SP was 68±8% lower than that of RAA → CS.

The foregoing is illustrative of the present invention, and is not to be construed as limiting thereof. The invention is defined by the following claims, with equivalents of the claims to be included therein.